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16dec06 11:51:06 User208760 Session D2801.1
                   0.133 DialUnits File1
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     $0.47 Estimated total session cost
                                          0.133 DialUnits
File 410:Dialog Comm.-of-Interest Newsl/Jul (c) 2006 Dialog
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? set hi ;set hi
HILIGHT set on as ''
HILIGHT set on as ''
? begin 5,73,155,399
       16dec06 11:51:19 User208760 Session D2801.2
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     $0.00 Estimated cost File410
     $0.05 TELNET
     $0.05 Estimated cost this search
     $0.52 Estimated total session cost 0.251 DialUnits
SYSTEM:OS - DIALOG OneSearch
        5:Biosis Previews(R) 1969-2006/Dec W2
  File
         (c) 2006 The Thomson Corporation
  File 73:EMBASE 1974-2006/Dec 15
         (c) 2006 Elsevier B.V.
  File 155:MEDLINE(R) 1950-2006/Dec 06
         (c) format only 2006 Dialog
*File 155: MEDLINE has temporarily stopped updating with UD=20061206.
Please see HELP NEWS154 for details.
  File 399:CA SEARCH(R) 1967-2006/UD=14524
         (c) 2006 American Chemical Society
*File 399: Use is subject to the terms of your user/customer agreement.
IPCR/8 classification codes now searchable as IC=. See HELP NEWSIPCR.
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? e au=wagner denisa ?
Ref
     Items Index-term
E1
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E2
         2 AU=WAGNER DENISA
E3
         0 *AU=WAGNER DENISA ?
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         1 AU=WAGNER DENNIS
         3 AU=WAGNER DENNIS L
E7
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       26 AU=WAGNER DIANE
E8
         9 AU=WAGNER DIANE R
E9
         3 AU=WAGNER DIANNE
E10
         1 AU=WAGNER DIAS CASALI, VICENTE
E11
        22 AU=WAGNER DIETER
E12
         Enter P or PAGE for more
? s e1-e4
              1 AU=WAGNER DENIS D
              2 AU=WAGNER DENISA
              0 AU=WAGNER DENISA ?
            162 AU=WAGNER DENISA D
            165 E1-E4
? s s1 and (cd62 or p(w)selectin or padgem or gmp140 or gmp(w)140)and (treat? or
therap? or administ?)(20n)(hemosta? or hemostati? or hemophilia or hypocoagula? or
hemorhagic or willebrand)
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            1012 GMP(W)140
         7807507 TREAT?
         7377013 THERAP?
         3960333 ADMINIST?
           81649 HEMOSTA?
           33762 HEMOSTATI?
           41061 HEMOPHILIA
            1167 HYPOCOAGULA?
              42 HEMORHAGIC
           43335 WILLEBRAND
           39446 ((TREAT? OR THERAP?) OR ADMINIST?)(20N)((((HEMOSTA? OR
                  HEMOSTATI?) OR HEMOPHILIA) OR HYPOCOAGULA?) OR
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      s3
               4 RD S2 (unique items)
? t s3/3/all
          (Item 1 from file: 5)
DIALOG(R) File 5: Biosis Previews(R)
(c) 2006 The Thomson Corporation. All rts. reserv.
0014921487
           BIOSIS NO.: 200400292244
A new role in hemostasis for the adhesion receptor P-selectin
AUTHOR: Cambien Beatrice; Wagner Denisa D (Reprint)
AUTHOR ADDRESS: Sch MedCtr Blood ResInst Biomed Res, Harvard Univ, Boston,
 MA, 02115, USA**USA
AUTHOR E-MAIL ADDRESS: wagner@cbr.med.harvard.edu
JOURNAL: Trends in Molecular Medicine 10 (4): p179-186 April 2004 2004
MEDIUM: print
ISSN: 1471-4914 (ISSN print)
DOCUMENT TYPE: Article; Literature Review
RECORD TYPE: Abstract
LANGUAGE: English
           (Item 2 from file: 5)
DIALOG(R) File 5: Biosis Previews(R)
(c) 2006 The Thomson Corporation. All rts. reserv.
            BIOSIS NO.: 200300390341
Interaction of P-selectin and PSGL-1 generates microparticles
  that correct hemostasis in a mouse model of hemophilia A.
AUTHOR: Hrachovinova Ingrid; Cambien Beatrice; Hafezi-Moghadam Ali;
 Kappelmayer Janos; Camphausen Raymond T; Widom Angela; Xia Lijun;
 Kazazian Haig H; Schaub Robert G; McEver Rodger P; Wagner Denisa D
  (Reprint)
AUTHOR ADDRESS: The Center for Blood Research and Department of Pathology,
```

Harvard Medical School, Boston, MA, 02115, USA\*\*USA AUTHOR E-MAIL ADDRESS: wagner@cbr.med.harvard.edu JOURNAL: Nature Medicine 9 (8): p1020-1025 August 2003 2003 MEDIUM: print ISSN: 1078-8956 (ISSN print) DOCUMENT TYPE: Article RECORD TYPE: Abstract LANGUAGE: English 3/3/3 (Item 3 from file: 5) DIALOG(R)File 5:Biosis Previews(R) (c) 2006 The Thomson Corporation. All rts. reserv. 0013616360 BIOSIS NO.: 200200209871 Soluble P-selectin shortens bleeding time by inducing tissue factor bearing microparticles in hemophilia A mice AUTHOR: Hrachovinova Ingrid (Reprint); Andre Patrick (Reprint); Kazazian Haig H; Wagner Denisa D (Reprint) AUTHOR ADDRESS: Center for Blood Research and Department of Pathology, Harvard Medical School, Boston, MA, USA\*\*USA JOURNAL: Blood 98 (11 Part 1): p446a November 16, 2001 2001 MEDIUM: print CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001; 20011207 SPONSOR: American Society of Hematology ISSN: 0006-4971 DOCUMENT TYPE: Meeting; Meeting Abstract RECORD TYPE: Abstract LANGUAGE: English 3/3/4 (Item 4 from file: 5) DIALOG(R) File 5: Biosis Previews(R) (c) 2006 The Thomson Corporation. All rts. reserv. 0012863218 BIOSIS NO.: 200100035057 Platelets adhere to and translocate on von Willebrand factor presented by endothelium in stimulated veins AUTHOR: Andre Patrick; Denis Cecile V; Ware Jerry; Saffaripour Simin; Hynes Richard O; Ruggeri Zaverio M; Wagner Denisa D (Reprint) AUTHOR ADDRESS: Center for Blood Research, 800 Huntington Ave, Boston, MA, 02115, USA\*\*USA JOURNAL: Blood 96 (10): p3322-3328 November 15, 2000 2000 MEDIUM: print ISSN: 0006-4971 DOCUMENT TYPE: Article RECORD TYPE: Abstract LANGUAGE: English ? s (cd62 or p(w)selectin or padgem or gmp140 or gmp(w)140) and (treat? or therap? or administ?) and (hemosta? or hemostati? or hemophilia or hypocoagula? or hemorhagic or willebrand) Processing Processing 1312 CD62 5346744 Ρ 42239 SELECTIN 17169 P(W) SELECTIN 5886 PADGEM 204 GMP140 81707 **GMP** 116915 140

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7807507 TREAT?
         7377013 THERAP?
         3960333 ADMINIST?
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           33762 HEMOSTATI?
           41061 HEMOPHILIA
            1167
                  HYPOCOAGULA?
              42 HEMORHAGIC
           43335 WILLEBRAND
      S4
             858
                 (CD62 OR P(W) SELECTIN OR PADGEM OR GMP140 OR GMP(W) 140)
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                  HEMOSTATI? OR HEMOPHILIA OR HYPOCOAGULA? OR HEMORHAGIC OR
                  WILLEBRAND)
? s s4 and hemophilia
             858 S4
           41061 HEMOPHILIA
      S5
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? rd s5
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      S6
              17 RD S5
? t s6/3/all
           (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2006 The Thomson Corporation. All rts. reserv.
0014921487
             BIOSIS NO.: 200400292244
A new role in hemostasis for the adhesion receptor P-
  selectin
AUTHOR: Cambien Beatrice; Wagner Denisa D (Reprint)
AUTHOR ADDRESS: Sch MedCtr Blood ResInst Biomed Res, Harvard Univ, Boston,
  MA, 02115, USA**USA
AUTHOR E-MAIL ADDRESS: wagner@cbr.med.harvard.edu
JOURNAL: Trends in Molecular Medicine 10 (4): p179-186 April 2004 2004
MEDIUM: print
ISSN: 1471-4914 _(ISSN print)
DOCUMENT TYPE: Article; Literature Review
RECORD TYPE: Abstract
LANGUAGE: English
          (Item 2 from file: 5)
 6/3/2
DIALOG(R)File
               5:Biosis Previews(R)
(c) 2006 The Thomson Corporation. All rts. reserv.
0014801739
            BIOSIS NO.: 200400172496
EM localization and agonist-induced release of human factor VIII from
  megakaryocytes transduced with a FVIII transgene.
AUTHOR: Wilcox David A (Reprint); Shi Qizhen (Reprint); Nurden Paquita;
 Haberichter Sandra L (Reprint); Rosenberg Jonathan B; Johnson Bryon D
  (Reprint); Nurden Alan T; White Gilbert C; Montgomery Robert R (Reprint)
AUTHOR ADDRESS: Department of Pediatrics, Medical College of Wisconsin,
 Milwaukee, WI, USA**USA
JOURNAL: Blood 102 (11): p87a-88a November 16, 2003 2003
MEDIUM: print
CONFERENCE/MEETING: 45th Annual Meeting of the American Society of
Hematology San Diego, CA, USA December 06-09, 2003; 20031206
SPONSOR: American Society of Hematology
ISSN: 0006-4971
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English
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1012 GMP(W)140

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(Item 3 from file: 5)
DIALOG(R) File 5:Biosis Previews(R)
(c) 2006 The Thomson Corporation. All rts. reserv.
0014431911 BIOSIS NO.: 200300390341
Interaction of P-selectin and PSGL-1 generates microparticles
                 ***hemostasis*** in a mouse model of
  that correct
                                                         ***hemophilia***
AUTHOR: Hrachovinova Ingrid; Cambien Beatrice; Hafezi-Moghadam Ali;
  Kappelmayer Janos; Camphausen Raymond T; Widom Angela; Xia Lijun;
  Kazazian Haig H; Schaub Robert G; McEver Rodger P; Wagner Denisa D
  (Reprint)
AUTHOR ADDRESS: The Center for Blood Research and Department of Pathology,
  Harvard Medical School, Boston, MA, 02115, USA**USA
AUTHOR E-MAIL ADDRESS: wagner@cbr.med.harvard.edu
JOURNAL: Nature Medicine 9 (8): p1020-1025 August 2003 2003
MEDIUM: print
ISSN: 1078-8956 (ISSN print)
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
 6/3/4
           (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2006 The Thomson Corporation. All rts. reserv.
           BIOSIS NO.: 200200218572
Platelet activation and hypercoagulability following treatment with
  porcine Factor VIII (HYATE:C)
AUTHOR: Freedman J (Reprint); Mody M; Lazarus A H; Dewar L; Song S;
 Blanchette V S; Garvey M B; Ofosu F A
AUTHOR ADDRESS: Transfusion Medicine, St. Michael's Hospital, 30 Bond St.,
  2 Victoria Wing, Toronto, ON, M5B 1W8, Canada**Canada
JOURNAL: American Journal of Hematology 69 (3): p192-199 March, 2002 2002
MEDIUM: print
ISSN: 0361-8609
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
           (Item 5 from file: 5)
DIALOG(R)File
               5:Biosis Previews(R)
(c) 2006 The Thomson Corporation. All rts. reserv.
           BIOSIS NO.: 200200209871
0013616360
Soluble P-selectin shortens bleeding time by inducing tissue
  factor bearing microparticles in hemophilia A mice
AUTHOR: Hrachovinova Ingrid (Reprint); Andre Patrick (Reprint); Kazazian
 Haig H; Wagner Denisa D (Reprint)
AUTHOR ADDRESS: Center for Blood Research and Department of Pathology,
 Harvard Medical School, Boston, MA, USA**USA
JOURNAL: Blood 98 (11 Part 1): p446a November 16, 2001 2001
MEDIUM: print
CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of
Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001; 20011207
SPONSOR: American Society of Hematology
ISSN: 0006-4971
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Abstract
```

Potential role of P-selectin glycoprotein ligand-1 in haematological diseases
Kappelmayer J.
Jugoslovenska Medicinska Biohemija ( JUGOSL. MED. BIOHEM. ) (Serbia and Montenegro) 2004, 23/3 (265-269)
CODEN: JMBIE ISSN: 0354-3447
DOCUMENT TYPE: Journal; Conference Paper
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH; SERBIAN
NUMBER OF REFERENCES: 8

6/3/9 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 2006 Elsevier B.V. All rts. reserv.

13746317 EMBASE No: 2006163682

```
Ways to bypass a blocked tenase complex
  Tuddenham E.G.D.
  E.G.D. Tuddenham, Faculty of Medicine, Imperial College, MRC Clinical
  Sciences Centre, Du Cane Road, London W12 ONN United Kingdom
  AUTHOR EMAIL: edward.tuddenham@csc.mrc.ac.uk
  Thrombosis and Haemostasis ( THROMB. HAEMOST. ) (Germany)
                                                               2006, 95/1
  (1-2)
  CODEN: THHAD
                 ISSN: 0340-6245
 DOCUMENT TYPE: Journal ; Editorial
  LANGUAGE: ENGLISH
  NUMBER OF REFERENCES: 11
 6/3/10
            (Item 3 from file: 73)
DIALOG(R) File 73: EMBASE
(c) 2006 Elsevier B.V. All rts. reserv.
             EMBASE No: 2004502845
  The Thr715Pro single nucleotide polymorphism of P-selectin:
Does it really matter in cardiovascular or thrombotic disorders?
  Jilma B.
  Dr. B. Jilma, Department of Clinical Pharmacology, Medical University
  Vienna, Waehringerguertel 18-20, A-1090 Vienna Austria
  Thrombosis and Haemostasis ( THROMB. HAEMOST. ) (Germany)
  (896 - 897)
  CODEN: THHAD
                 ISSN: 0340-6245
 DOCUMENT TYPE: Journal ; Editorial
 LANGUAGE: ENGLISH
  NUMBER OF REFERENCES: 15
            (Item 4 from file: 73)
DIALOG(R) File 73: EMBASE
(c) 2006 Elsevier B.V. All rts. reserv.
12460521
             EMBASE No: 2004056085
 P-selectin modulation in haemostasis: One size fits all?
  Grunewald M.; Griesshammer M.
 M. Grunewald, Department of Medicine III, Haemostasis Division,
 University of Ulm, Robert-Koch-Strasse 8, D-89081 Ulm Germany
 AUTHOR EMAIL: martin.gruenewald@medizin.uni-ulm.de
 Trends in Molecular Medicine ( TRENDS MOL. MED. ) (United Kingdom)
                                                                        2004
, 10/1 (9-12)
 CODEN: TMMRC
                ISSN: 1471-4914
 DOCUMENT TYPE: Journal ; Review
 LANGUAGE: ENGLISH
                      SUMMARY LANGUAGE: ENGLISH
 NUMBER OF REFERENCES: 19
            (Item 5 from file: 73)
DIALOG(R) File 73: EMBASE
(c) 2006 Elsevier B.V. All rts. reserv.
11392048
            EMBASE No: 2001406270
 Regulated secretion in endothelial cells: Biology and clinical
implications
 Datta Y.H.; Ewenstein B.M.
 Prof. Dr. Y.H. Datta, Division of Hematology/Oncology, Medical College of
 Wisconsin, 9200 W. Wisconsin Avenue, Milwaukee, WI 53226 United States
 AUTHOR EMAIL: yhdatta@mcw.edu
 Thrombosis and Haemostasis ( THROMB. HAEMOST. ) (Germany)
  (1148-1155)
```

CODEN: THHAD ISSN: 0340-6245 DOCUMENT TYPE: Journal; Review

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 93

6/3/13 (Item 6 from file: 73)

DIALOG(R) File 73: EMBASE

(c) 2006 Elsevier B.V. All rts. reserv.

07645412 EMBASE No: 1999135564

Plasma platelet-activating factor (PAF) levels and desmopressin response in children with hemophilia A and von Willebrand's disease [8]

Kavakli K.; Polat A.; Huseyinof A.; Nisli G.; Aydinok Y.

Dr. K. Kavakli, Department of Pediatric Hematology, Ege University

Hospital, TR-35100 Bornova, Izmir Turkey

AUTHOR EMAIL: Kkavakli@med.ege.edu.tr

Thrombosis and Haemostasis (THROMB. HAEMOST.) (Germany) 1999, 81/4

(665-666)

CODEN: THHAD ISSN: 0340-6245 DOCUMENT TYPE: Journal; Letter

LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 7

6/3/14 (Item 7 from file: 73)

DIALOG(R) File 73: EMBASE

(c) 2006 Elsevier B.V. All rts. reserv.

07534175 EMBASE No: 1998378671

A possible mechanism of action of activated factor VII independent of tissue factor

Monroe D.M.; Hoffman M.; Oliver J.A.; Roberts H.R.

Dr. D.M. Monroe, University of North Carolina, Hematology/Oncology, 932 Mary Ellen Jones Building, Chapel Hill, NC 27599-7035 United States

AUTHOR EMAIL: dmonroe@med.unc.edu

Blood Coagulation and Fibrinolysis (BLOOD COAGUL. FIBRINOLYSIS ) (United

Kingdom) 1998, 9/SUPPL. 1 (S15-S20)

CODEN: BLFIE ISSN: 0957-5235

DOCUMENT TYPE: Journal; Conference Paper

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 28

6/3/15 (Item 1 from file: 155)

DIALOG(R) File 155: MEDLINE(R)

(c) format only 2006 Dialog. All rts. reserv.

14425544 PMID: 12894156

Coaxing coagulation with RNA and cell fragments.

High Katherine A

Nature medicine (United States) Aug 2003, 9 (8) p991-2, ISSN 1078-8956--Print Journal Code: 9502015

Publishing Model Print; Comment on Nat Med. 2003 Aug;9(8) 1015-9; Comment on PMID 12847523; Comment on Nat Med. 2003 Aug;9(8):1020-5; Comment on PMID 12858167

Document type: Comment; News

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

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6/3/16
            (Item 2 from file: 155)
DIALOG(R) File 155: MEDLINE(R)
 (c) format only 2006 Dialog. All rts. reserv.
14405787
           PMID: 12871503
   The P-selectin cytoplasmic domain directs the cellular
storage of a recombinant chimeric factor IX.
  Plantier J-L; Enjolras N; Rodriguez M-H E; Masse J-M; Cramer E M; Negrier
  INSERM U331, Laboratoire d'Hemobiologie-Faculte de Medecine RTH, Laennec,
Lyon, France.
  Journal of thrombosis and haemostasis - JTH (England)
                                                           Feb 2003, 1 (2)
  p292-9, ISSN 1538-7933--Print Journal Code: 101170508
  Publishing Model Print
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: MEDLINE; Completed
 6/3/17
            (Item 1 from file: 399)
DIALOG(R) File 399:CA SEARCH(R)
(c) 2006 American Chemical Society. All rts. reserv.
  136000640
               CA: 136(1)640k
                                 PATENT
  Methods for diagnosing and treating hemostatic disorders by modulating
  P-selectin activity
  INVENTOR(AUTHOR): Wagner, Denisa D.; Andre, Patrick; Hartwell, Daqing W.;
Hrachovinova, Ingrid
  LOCATION: USA
  ASSIGNEE: The Center for Blood Research
  PATENT: PCT International; WO 200189564 A2 DATE: 20011129
  APPLICATION: WO 2001US16021 (20010517) *US PV205734 (20000519)
  PAGES: 93 pp. CODEN: PIXXD2 LANGUAGE: English
  PATENT CLASSIFICATIONS:
    CLASS: A61K-039/395A; A61K-048/00B; A61K-038/17B; A61K-035/14B;
A61P-007/00B; A61P-009/00B; A61P-035/00B; G01N-033/50B; G01N-033/86B;
G01N-033/68B
  DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ;
CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DZ; EC; EE; ES; FI; GB; GD; GE; GH;
GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU;
LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI;
SK; SL; TJ; TM; TR; TT; TZ; UA; UG; UZ; VN; YU; ZA; ZW; AM; AZ; BY; KG; KZ;
MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW; MZ; SD; SL; SZ; TZ
; UG; ZW; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL;
PT; SE; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GW; ML; MR; NE; SN; TD; TG
? t s6/7/1,3,4,5,8,11,13,16
           (Item 1 from file: 5)
DIALOG(R) File 5:Biosis Previews(R)
(c) 2006 The Thomson Corporation. All rts. reserv.
0014921487
             BIOSIS NO.: 200400292244
A new role in hemostasis for the adhesion receptor P-
AUTHOR: Cambien Beatrice; Wagner Denisa D (Reprint)
AUTHOR ADDRESS: Sch MedCtr Blood ResInst Biomed Res, Harvard Univ, Boston,
  MA, 02115, USA**USA
AUTHOR E-MAIL ADDRESS: wagner@cbr.med.harvard.edu
JOURNAL: Trends in Molecular Medicine 10 (4): p179-186 April 2004 2004
MEDIUM: print
ISSN: 1471-4914 (ISSN print)
```

DOĆUMENT TYPE: Article; Literature Review

RECORD TYPE: Abstract LANGUAGE: English

ABSTRACT: The adhesion receptor P-selectin has long been known to support leukocyte rolling and emigration at sites of inflammation. Recently, P-selectin was also revealed to be a key molecule in hemostasis and thrombosis, mediating platelet rolling, generating procoagulant microparticles containing active tissue factor and enhancing fibrin deposition. Elevated levels of plasma selectin are indicative of thrombotic disorders and predictive of future cardiovascular events. Because the interaction between \*\*\*p\*\*\* selectin and its receptor P-selectin glycoprotein ligand-1 (PSGL-1) represents an important mechanism by which Pselectin induces the formation of procoagulant microparticles and recruits the microparticles to thrombi, anti-thrombotic strategies are currently aimed at inhibiting this interaction. Recent developments also suggest that the procoagulant potential of P-selectin could \*\*\*treat\*\*\* coagulation disorders such as \*\*\*hemophilia\*\*\*

6/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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0014431911 BIOSIS NO.: 200300390341
Interaction of P-selectin and PSGL-1 generates microparticles
that correct \*\*\*hemostasis\*\*\* in a mouse model of \*\*\*hemophilia\*\*\* A
AUTHOR: Hrachovinova Ingrid; Cambien Beatrice; Hafezi-Moghadam Ali;
Kappelmayer Janos; Camphausen Raymond T; Widom Angela; Xia Lijun;
Kazazian Haig H; Schaub Robert G; McEver Rodger P; Wagner Denisa D
(Reprint)

AUTHOR ADDRESS: The Center for Blood Research and Department of Pathology,
Harvard Medical School, Boston, MA, 02115, USA\*\*USA

AUTHOR E-MAIL ADDRESS: wagner@cbr.med.harvard.edu

JOURNAL: Nature Medicine 9 (8): p1020-1025 August 2003 2003

MEDIUM: print

ISSN: 1078-8956 (ISSN print)

DOCUMENT TYPE: Article RECORD TYPE: Abstract LANGUAGE: English

ABSTRACT: High plasma levels of soluble P-selectin are associated with thrombotic disorders and may predict future cardiovascular events. Mice with high levels of soluble selectin have more microparticles in their plasma than do normal \*\*\*P\*\*\* - \*\*\*selectin\*\*\* mice. Here we show that chimeras of and immunoglobulin (P-sel-Ig) induced formation of procoagulant microparticles in human blood through P-selectin glycoprotein ligand-1 (PSGL-1; encoded by the Psgl1 gene, officially known as Selpl). In addition, Psgll-/- mice produced fewer microparticles after P-sel-Ig infusion and did not spontaneously increase their microparticle count in old age as do wild-type mice. Injected microparticles specifically bound to thrombi and thus could be involved in thrombin generation at sites of injury. Infusion of P-sel-Ig into \*\*\*hemophilia\*\*\* A mice produced a 20-fold increase over control immunoglobulin in microparticles containing tissue factor. This significantly improved the kinetics of fibrin formation in the hemophilia A mice and normalized their tail-bleeding time. P-sel-Ig \*\*\*treatment\*\*\* could become a new approach to sustained control of bleeding in \*\*\*hemophilia\*\*\*

(Item 4 from file: 5) DIALOG(R) File 5: Biosis Previews (R) (c) 2006 The Thomson Corporation. All rts. reserv.

0013625061 BIOSIS NO.: 200200218572 Platelet activation and hypercoagulability following treatment with porcine Factor VIII (HYATE:C)

AUTHOR: Freedman J (Reprint); Mody M; Lazarus A H; Dewar L; Song S; Blanchette V S; Garvey M B; Ofosu F A

AUTHOR ADDRESS: Transfusion Medicine, St. Michael's Hospital, 30 Bond St., 2 Victoria Wing, Toronto, ON, M5B 1W8, Canada\*\*Canada

JOURNAL: American Journal of Hematology 69 (3): p192-199 March, 2002 2002

MEDIUM: print ISSN: 0361-8609

DOCUMENT TYPE: Article RECORD TYPE: Abstract LANGUAGE: English

ABSTRACT: Activation of platelets and coagulation in vivo was studied in nine patients with hemophilia A and inhibitors to human Factor VIII, prior to and following treatment with porcine Factor VIII (PFVIII; HYATE:C). In addition, six hemophiliac patients were similarly \*\*\*treatment\*\*\* with recombinant Factor VIII (rFVIII). studied after Platelet activation was also examined in vitro using porcine von Willebrand factor (PvWF)-enriched and PvWF-depleted fractions obtained by fractionation of PFVIII. Coagulation was assessed by measuring the concentrations of plasma prothrombin fragment 1+2 concentrations (prothrombinase generation) and Factor Xa-ATIII. Patients treated with PFVIII had significantly increased numbers of circulating platelets expressing CD62 and CD63 (markers of platelet activation) and annexin V (marker of platelet procoagulant activity) compared to patients treated with rFVIII; the former patients also demonstrated an increase in plasma coagulability after in vitro experiments it was observed that the platelet-activating and procoagulant capacity of PFVIII resided in the PvWF-enriched fraction, and the same was true for the plasma hypercoagulability following exposure of platelets to PFVIII. These results support the hypothesis that PFVIII-induced platelet activation provides a mechanism for enhancing hemostasis, separate from, and additional to, that due to increased circulating Factor VIII, and it is due to residual PvWF in the PFVIII preparation.

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Soluble P-selectin shortens bleeding time by inducing tissue factor bearing microparticles in hemophilia A mice

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ABSTRACT: Previously we reported that soluble P-selectin (sP-sel) is a direct inducer of pro-coagulant activity, as it promotes the formation of pro-coagulant microparticles in blood (Andre, P., Hartwell, D., Hrachovinova, I., Saffaripour, S., and Wagner, D.D. PNAS, 2000, 97:13835-13840). Since some of these microparticles express tissue factor (TF), we decided to investigate the possible therapeutic potential of sP-sel in treatment of hemostatic defects present in factor FVIII-/- mice ( \*\*\*hemophilia\*\*\* hemophilia A, thrombin generation depends on the factor VII/TF \*\*\*Hemophilia\*\*\* pathway, since factor VIII is deficient. A mice (Bi, L., Lawler, A.M., Antonarakis, S.E., High, K.A., Gearhart, J.D., Kazazian, H. H. Nature Genetics, 1995, 10:119-121) were injected in tail vein with soluble murine P-selectin-Ig (P-sel-Ig) chimera or IgG1 control (1.2 mug/g body weight) and we measured tail bleeding time six hours later. All P-sel-Ig \*\*\*treated\*\*\* mice (n=8) stopped bleeding within three minutes (1.5+-0.25 min), while five out of eight IgG1treated mice did not stop bleeding by 15 minutes when their tails were cauterized. Thus bleeding time was significantly (p<0.005) shorter in P-sel-Ig injected mice than in IgG1 controls. In another experiment eleven hemophilia A mice infused with P-sel-Ig and seven mice infused with IgG1 were bled into ACD six hours after \*\*\*treatment\*\*\* Activated partial thromboplastin time (APTT) and recalcified clotting time were determined in platelet poor plasma. Both APTT and clotting time were significantly shorter (p<0.006) in P-sel-Ig \*\*\*treated\*\*\* Shorter APTT in P-sel-Ig \*\*\*treated\*\*\* mice (31.7+-0.7 vs. 37.9+-1.6 seconds) indicates a higher level of TF-bearing microparticles in plasma. To verify this, microparticles were isolated from the plasma, stained for TF and flow cytometry analysis was performed. 10,000 events were counted to determine the population of TF-positive microparticles. We found that hemophilia A mice treated with P-sel-Ig had, on average, seven times more TF-positive microparticles (14.2+-1.65%) than mice \*\*\*treated\*\*\* with IgG1 (1.9+-0.3%). The difference was statistically significant (p<0.001). We conclude that sP-sel can improve bleeding and coagulation parameters in hemophilia A mice and thus could be considered as an adjunctive treatment for patients with a congenital bleeding disorder such as \*\*\*hemophilia\*\*\* .

6/7/8 (Item 1 from file: 73) DIALOG(R) File 73: EMBASE (c) 2006 Elsevier B.V. All rts. reserv. EMBASE No: 2004411429 Potential role of P-selectin glycoprotein ligand-1 in haematological diseases Kappelmayer J. Jugoslovenska Medicinska Biohemija ( JUGOSL. MED. BIOHEM. ) (Serbia and Montenegro) 2004, 23/3 (265-269) ISSN: 0354-3447 CODEN: JMBIE DOCUMENT TYPE: Journal ; Conference Paper LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH; SERBIAN NUMBER OF REFERENCES: 8

PSGL-1 is a major counterreceptor of all three types of selectins that is expressed in several leukocyte subsets. Data presented, here prove that this mucin may be implied in haematological disorders. We established on normal peripheral blood and in samples derived from 20 AML patients that PSGL-1 is differently expressed in various leukocyte subsets. Myeloblasts appearing in acute myeloid leukaemia patients express significantly less PSGL-1 (12 000 +/- 5300) than mature neutrophils (p < 0.001). In monocytic

leukaemias, however, the amount of PSGL-1 on monocytic precursors is displayed in a fairly broad range which was not significantly different from that of mature monocytes (p=0.084). Monoblasts/promononocytes possess more PSGL-1 than myeloblasts and the expression pattern is completely non-overlapping. This would imply a differential expression of PSGL-1 during myeloid haemopoietic development and suggests, that the quantitation of surface PSGL-1 may help in differentiating myeloblasts from monoblasts by immunophenotyping in different AML subsets. PSGL-1 has also a certain role in the generation of procoagulant microparticles (MP) as in the PSGL-1 knockout mouse the MP number failed to increase with age and the MP contained significantly less tissue factor than wild type mice. Since PSGL-1 P-selectin interaction is crucial in generating a procoagulant effect we tested the hypothesis that the administration of a P-selectin IgG chimera (Psel-lg) corrects bleeding tendency in a murine haemophilia model and in human haemophilic blood. The addition of Psel-lg resulted in significant improvement of the bleeding tendency in mice and in the generation of MP in human hemophilic blood. Thus, the Psel-lg can become an alternative route to control bleeding tendency in coagulopathies.

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NUMBER OF REFERENCES: 19

12460521 EMBASE No: 2004056085
P-selectin modulation in haemostasis: One size fits all?
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Trends in Molecular Medicine (TRENDS MOL. MED.) (United Kingdom) 2004
, 10/1 (9-12)
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LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Haemostasis and inflammation are tightly linked reactions primarily designated as post-traumatic protection mechanisms. Both reactions require the recruitment of specialized cells with specific functions. Recruitment of cells from circulating blood is a precisely regulated, receptor-mediated process that prevents inadvertent (e.g. thrombosis) and insufficient (e.g. bleeding) effects. \*\*\*P\*\*\* - \*\*\*selectin\*\*\* is a leukocyte-adhesion receptor but is also expressed on platelet and endothelial cell surfaces. It promotes interactions of leukocytes with platelets and endothelial cells,

but is also expressed on platelet and endothelial cell surfaces. It promotes interactions of leukocytes with platelets and endothelial cells, enabling leukocyte and platelet rolling on activated endothelial surfaces. Endothelial rolling of circulating cells represents an intermediate step before firm adhesion that still enables detachment.

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DIALOG(R)File 73:EMBASE
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07645412 EMBASE No: 1999135564
Plasma platelet-activating factor (PAF) levels and desmopressin response in children with hemophilia A and von Willebrand's disease [8]
Kavakli K.; Polat A.; Huseyinof A.; Nisli G.; Aydinok Y.
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Thrombosis and Haemostasis (THROMB. HAEMOST.) (Germany) 1999, 81/4 CODEN: THHAD ISSN: 0340-6245 DOCUMENT TYPE: Journal; Letter LANGUAGE: ENGLISH NUMBER OF REFERENCES: 7 6/7/16 (Item 2 from file: 155) DIALOG(R) File 155: MEDLINE(R) (c) format only 2006 Dialog. All rts. reserv. 14405787 PMID: 12871503 The P-selectin cytoplasmic domain directs the cellular storage of a recombinant chimeric factor IX. Plantier J-L; Enjolras N; Rodriguez M-H E; Masse J-M; Cramer E M; Negrier INSERM U331, Laboratoire d'Hemobiologie-Faculte de Medecine RTH, Laennec, Lyon, France. Journal of thrombosis and haemostasis - JTH (England) Feb 2003, 1 (2) p292-9, ISSN 1538-7933--Print Journal Code: 101170508 Publishing Model Print Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: MEDLINE; Completed Hemophilia B was recognized as a good candidate for gene \*\*\*therapy\*\*\* . Several strategies have been attempted and gave promising results in hemophilic animals but failed to achieve corrective levels in humans. To overcome this inconvenience we aimed to generate intracellular pools of factor (F) IX in cells that are implicated in the hemostatic response, e.g. endothelial cells and platelets. Upon stimulation, these cells release their granule content, which in this case would result in an increase in local FIX concentration, and could locally produce an effective \*\*\*hemostasis\*\*\* . In an attempt to produce an intracellular pool of releasable coagulation FIX, the cytoplasmic domain of the Pselectin (pselCT) molecule was fused to the carboxy-terminal extremity of the human FIX protein. The properties of this chimeric molecule (FIX-pselCT) were studied in AtT20, a cell line which possesses storage granules. As previously shown for transmembrane molecules but not for a soluble protein such as FIX, the pselCT fragment induces the storage of FIX-pselCT. The coagulant activity of FIX-pselCT was not affected by the addition of the pselCT tail. The \*\*\*treatment\*\*\* of AtT20 cells with inhibitors revealed that FIX-pselCT was not submitted to different intracellular degradation and that the half-life of the chimeric molecule was at least two times longer than that of FIX-WT. An immunoelectron microscopic analysis demonstrated a specific localization of FIX-pselCT the ACTH-containing granules. Cell stimulation using Phorbol Myristrate Acetate (PMA), ionophore A-23187 or 8-Br-cAMP induced efficient release of an active FIX-pselCT. These data demonstrate that the addition of the cytoplasmic domain of P-selectin to FIX modifies the cellular fate of the FIX molecule by directing the recombinant protein  ${\bf r}$ 

toward regulated-secretory granules without altering its coagulant

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